REMARKS

These remarks are in response to the Office Action mailed July 6, 2001. Applicants gratefully acknowledge the Examiner's suggestions regarding certain claim amendments. Additionally, the Applicants acknowledge the Examiner's conclusion that claims 4-11 would be allowable if rewritten in independent form. Newly added claim 33 represents claims 4-11 rewritten in independent form in which the individual enzymes of SEQ ID NOS: 25-32 are included in a grouping rather than claimed individually.

The Office Action rejected claims 1-3, 13, and 14 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 09/412,184. Applicants ask for a delay in responding to this double patenting rejection until the claims of the present application are found to be allowable, or until issuance of the 09/412,184 application.

Claims 1-14 and 17-24 were pending before this response. By the present communication, claims 1, 12, 17, and 22 are amended to define Applicants' invention with greater particularity, and new claims 25-35 have been added. These amendments and additions add no new matter as the claim language is fully supported by the specification and original claims. Accordingly, claims 1-14 and 17-35 are pending, as shown in attached Exhibit A.

The Rejection under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection of claims 1-3, 13, 14, and 17-24 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the Specification in such a way as to reasonably convey that the inventors had possession of the invention at the time of filing of the Application. In particular, with respect to claims 1-3, 13, and 14, the Office Action asserts that the rejected claims cover too diverse a class of enzymes, in not indicating the specificity of the aminotransferase encompassed by the claims. Therefore, it is

alleged that the specific transaminases having an amino acid sequence that is 70% identical to such sequences are unknown.

Claims 1-3, 13, and 14 have been amended to more clearly define the invention. Claim 1, to which claims 2-3, 13, and 14 depend, is amended herein to further clarify that it is directed to polynucleotides that encode an enzyme with aminotransferase activity wherein the amino acid sequence is 70% identical to SEQ ID NOS:25-32. Therefore, the claims include both a structural and a functional limitation. Nothing more is required to meet 35 U.S.C. 112, first paragraph, for biomolecules of this type.

The Office Action indicates that the functional limitation should limit the claimed polynucleotides to those encoding aminotransferases with the same donors and acceptors as the disclosed enzymes. However, such a limitation is too narrow and would open the floodgates for potential infringers to use the teachings of the present application to devise polynucleotides that encode an amino acid sequence related to SEQ ID NO:25-32 but that have different donor or acceptor specificity. Like many if not all enzymes, the aminotransferases of SEQ ID NOS:25-32 catalyze reactions to attain specific products from specific reactants. Therefore, the written description requirement under 35 U.S.C. 112, first paragraph should be no different than for similar claims directed to polynucleotides encoding other enzymes, which requires a structural limitation and a functional limitation related to the activity of the enzyme, as provided herein. Based on the teachings of the present disclosure, one of ordinary skill in the art recognizes that the amino acid sequence of the enzyme can likely be modified to be at least 70% identical to SEQ ID NOS: 25-32 yet retain aminotransferase activity, possibly with different amino group donor and/or acceptor specificity. Therefore, the written description requirement is met for claims 1-3, 13, and 14. Accordingly, reconsideration and withdrawal of the rejection of claims 1-3, 13, and 14 are respectfully requested.

It is noteworthy that newly added claim 34 is directed to polynucleotides that encode polypeptides with the same amino group acceptor and amino group donor specificity as the aminotransferase of SEQ ID NOS:25-32 to which they have 70% sequence identity. Therefore,

despite the fact that Applicants assert that the claims do NOT need to be limited to the same donor and acceptor specificity as the aminotransferases of SEQ ID NOS: 25-32, the invention of this claim is limited in this manner.

With respect to claims 17-24, the Office Action objects to the Specification as not providing adequate written description of these claims based on similar assertions to those described above regarding claims 1-3, 13 and 14. More specifically, regarding claims 17-24, the Office Action asserts that the specific function of a polypeptide encoded by a nucleic acid that hybridizes under the conditions recited in claim 17 with a probe of 10-50 nucleotides that is 70% complementary to a DNA encoding SEQ ID Nos:25-32 would be unpredictable. Furthermore, the Office Action asserts that claims 17-24 are not adequately described because a structural limitation is imparted in the claimed nucleic acids but there is no functional limitation.

Claims 17-24 are directed to nucleic acid probes of 10-50 nucleotides that are at least 70% complementary to target regions of polynucleotides that encode the aminotransferases of SEQ ID NOS:25-32 under specified conditions. The function of the nucleic acid probes is not necessarily to encode full length transaminase enzymes with a particular specificity. Rather, the function of the nucleic acid probes as indicated in the claims, is to form target:probe duplexes under certain specified conditions (i.e. to function as probes). Thus, a probe as in claims 17-24 can be used, for example, for recovery of the polynucleotides of SEQ ID NOS:17-24, as a diagnostic probe, or as a PCR primer (*See* specification as filed page 12, third paragraph, lines 4-7). Therefore, the nucleic acid probes of claims 17-24 are adequately described by the specification as filed, and need not be limited regarding the specificity of transaminase activity. Furthermore, regarding claims 19, 20, and 21, these claims are directed to nucleic acids having increasing complementarity to nucleic acid target regions of SEQ ID NOS: 25-32, up to, and including 100% complementarity (*see* claim 21). Therefore, the claims are directed to various nucleic acid probes, including nucleic acid probes whose sequence is provided in the specification (i.e., 100% complementary to a portion of SEQ ID NOS:25-32, Claim 21). Accordingly, reconsideration and withdrawal of the rejection of claims 17-24 is respectfully requested.

Applicants respectfully traverse the rejection of claims 1-3, 13, 14 and 17-24 under 35 U.S.C. §112, first paragraph, for allegedly lacking an enabling description in the Specification.

Applicants respectfully traverse the rejection of claims 1-3, 13, 14, and 17-24 under 35 U.S.C. § 112, first paragraph. Allegedly, the specification does not reasonably provide enablement for a polynucleotide encoding an aminotransferase of unspecified specificity having an amino acid sequence 70% identical to SEQ ID Nos:25-32 and a probe of 10-50 nucleotides that is 70% complementary to a polynucleotide encoding SEQ ID NOs: 25-32. The Office Action asserts that knowledge of which residues can be altered or removed, so that they retain 70% identity and result in an unspecified aminotransferase activity is well outside routine experimentation. Furthermore, the Office Action asserts that the function, substrate, and stereo-specificity is unpredictable for an aminotransferase with an amino acid sequence 70% identical to SEQ ID NOS: 25-32.

Claims 1-3, 13, and 14 recite polynucleotides encoding polypeptides with the same amino group acceptor and amino group donor specificity as the aminotransferase of SEQ ID NO:25-32 to which they have 70% sequence identity. Accordingly, reconsideration and withdrawal of the rejection of claims 1-3, 13, and 14 are respectfully requested.

Regarding the nucleic acid of claims 17-24, the Office Action asserts that the specification does not teach the function of all polypeptides encoded by a polynucleotide that hybridizes with a 10-50 nucleotide probe that is 70, 90 or 95% complementary to the target DNA. Furthermore, the Office Action asserts that "without knowing the function, one of ordinary skill in the art would not know how to use a polypeptide." Finally, the Office Action asserts that one skilled in the art would require guidance as to how use a probe that is 70, 90 or 95% complementary to an unspecified area of a DNA encoding SEQ ID NOs: 25-32 that hybridizes to a DNA encoding a polypeptide of unknown function in a manner reasonably correlated with the scope of the claims. Without such guidance, the Office Action indicates that experimentation left to those skilled in the art is undue.

The specification adequately teaches one skilled in the art how to make and use the nucleic acid probe of claims 17-24. One of ordinary skill can use routine procedures to make a nucleic acid probe 10-50 nucleotides in length. For example, the probe can be synthesized using well-known and commercially-available nucleic acid synthesizers. As in the written description rejection discussed above, the Office Action again incorrectly focuses on the function of a polypeptide, rather than the function of the claimed probe. The function of the nucleic acid probe is not related to encoding transaminase enzymes with certain specificity. Rather, the function of the nucleic acid probes, as indicated in the claims, is to form target:probe duplexes under certain specified conditions (i.e. to function as a probe). The probe can be used, for example, for recovery of the polynucleotides of SEQ ID NOS:17-24, for diagnostic purposes, or as a PCR primer (specification as filed page 12, third paragraph, lines 4-7). Therefore, the specification teaches an ordinary artisan how to make and use the claimed invention.

Applicants respectfully submit, therefore, that those of average skill in the art could use the techniques disclosed in the Specification and known in the art as of the filing date of the present application to make and use the invention, as defined by amended claims 1-3, 13, 14 and 17-24 without undue experimentation. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse the rejection of claims 1, 12, and 17-24 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. With regard to the alleged indefiniteness of claim 1(b), claim 1 has been amended to delete clause (b) from claim 1, thus obviating the rejection as to this point. With regard to the alleged indefiniteness of claim 1(c), claim 1 has been amended to clarify that the polynucleotide of claim 1 either encodes an enzyme with aminotransferases activity and which is at least 70% identical to SEQ ID NOS:25-32, wherein the enzyme encoded by the isolated polynucleotide has the same amino group acceptor and amino group donor specificity as the enzyme to which it is at least 70% identical, or the

polynucleotide is complementary to the polynucleotide that encodes an enzyme with aminotransferases activity and which is at least 70% identical to SEQ ID NOS:25-32, wherein the enzyme encoded by the isolated polynucleotide has the same amino group acceptor and amino group donor specificity as the enzyme to which it is at least 70% identical. Therefore, the Office Action's assertion that clause (c) is indefinited, have been overcome.

Regarding the alleged indefiniteness of the term "an enzyme with aminotransferase activity" in claim 1, the applicants traverse the Office Action assertion that this term is unascertainable because it is unclear which enzymes other than aminotransferases, are included in the scope of the claim. As an initial clarification, this claim is directed to polynucleotides encoding enzymes with aminotransferase activity. The claim language itself is clear that all of the enzymes encoded by a polynucleotide of claim 1 have aminotransferase activity. Methods are readily available for determining whether an enzyme has aminotransferase activity. Therefore, one of ordinary skill can readily ascertain whether a polynucleotide encodes an enzyme with aminotransferase activity, and therefore is within this limitation of the claim. Thus, the phrase "an enzyme with aminotransferase activity" does not render claim 1 indefinite.

Regarding the Office Action's assertion regarding indefiniteness of claim 12, this claim has been amended to recite "in any one of SEQ ID NOS: 17-24" as suggested in the Office Action.

Regarding the alleged indefiniteness of the phrase "about 10 to 50 nucleotides" in claim 17, applicants traverse the Office Action's assertion that the use of "about" renders the metes and bounds of the claim unascertainable. MPEP 2173.05(b)A states that the term "about" is not indefinite in some instances. That section of the MPEP cites W.L. Gore & Associates, Inc. V Garlock Inc., 220 USPQ 303, 316 (C.A.F.C. 1983), in which it was held that the claim language "stretching... at a rate exceeding *about* 10% per second" (emphasis added) is not indefinite. The court reasoned that "[I]nfringement is clearly assessable through use of a stopwatch," and therefore the claim is not indefinite under 35 U.S.C. 112, second paragraph. Gore, 220 USPQ at 216. In the same vein, the use of the term "about" in claim 17 is clearly assessable by simply

counting the number of nucleotides in a complementary oligonucleotide of the probe and determining whether the number of nucleotides in this oligonuclteotide is between 10 to 50 nucleotides or is a size that an ordinary artisan would consider equivalent to 10 to 50 nucleotides with respect to a probe and its hybridization to a target region. Moreover, Applicants respectfully point out that the use of "about" in claim 17 is consistent with, and sanctioned by, current claim drafting standards in the United States. The Office Action has not presented any discussion concerning how Applicants' use of the qualifier "about" differs from the use in claims issued and allowed by the USPTO virtually every working day.

Regarding the alleged indefiniteness of the phrase "an area of nucleotides that is at least 70% complementary" in claim 17, applicants traverse the Office Action's assertion that it is unclear whether the area is the entire probe or a fragment thereof. Applicants have amended claim 17 to indicate that it is a "region" of the probe that is at least 70% complementary to a nucleic acid target region. It is clear from the language of the claim and the knowledge of an ordinary artisan, that the complementary region can be either the entire nucleic acid or a portion thereof. If the complementary region was intended to be limited to the entire probe, the phrase would not be included in the claim. If the claim was intended to be limited to probes which have only portions that are 70% complementary to a nucleic acid target region, then the claim would have specified this. Therefore, it is clear to an ordinary artisan that the phrase "a region of nucleotides that is at least 70% complementary" covers nucleic acid probes in which the entire probe, or a fragment thereof, is complementary to a nucleic acid target region.

Regarding a lack of antecedent bases for "bases" in claim 22, this claim has been amended herein to change "bases" to "nucleotides," which has antecedent basis.

In view of these amendments, Applicants respectfully submit that claims 1-14 and 17-24 meet all requirements under 35 U.S.C. § 112, second paragraph.

In view of the above amendments and remarks, reconsideration and favorable action on claims 1-14 and 17-24 are respectfully requested. In the event any matters remain to be resolved

in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

In view of the above remarks, reconsideration and favorable action on all claims is respectfully requested. Should any questions remain in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Attachment – Exhibit A

EXHIBIT A

VERSION WITH MARKINGS

1. (Twice amended) An isolated polynucleotide selected from:

a) a polynucleotide encoding an enzyme with aminotransferases activity [and which] wherein the amino acid sequence of the enzyme is at least 70% identical to [a member selected from the group consisting of:

a)] SEQ ID NOS:25-32; and

b) [SEQ ID NOS:25-32 wherein T can also be U; and

c)] a polynucleotide comprising a nucleic acid sequence[s] complementary to a polynucleotide of a)[and b)].

12. (Amended) The polynucleotide[s] of claim 1 comprising any one of the sequences as set forth in SEQ ID NOS:17-24.

17. (Amended) A nucleic acid probe comprising an oligonucleotide from about 10 to 50 nucleotides in length and having a[n area] region of nucleotides that is at least 70% complementary to a nucleic acid target region of a nucleic acid encoding an amino acid sequence selected from the group consisting of SEQ ID NOS:25-32 and which hybridizes to the nucleic acid target region to form a detectable target:probe duplex under conditions that include 0.9 M NaC1, 5.0 mM NaH_2PO_4, 5.0 mM Na_2 EDTA, 0.5% SDS and 10 X Denhardt's at about 45° C.

22. (Amended) The probe of claim 17, wherein the oligonucleotide is 15-50 [bases] nucleotides in length.

Please add the following new claims:

--25. The polynucleotide of claim 2 which encodes an aspartate transaminase that is at least 70% identical to the enzyme of SEQ ID NO:25.

26. The polynucleotide of claim 2 which encodes an aspartate aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:26.

27. The polynucleotide of claim 2 which encodes an adenosyl-8-amino-7oxononanoate aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:27.

28. The polynucleotide of claim 2 which encodes an acetylornithine aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:28.

29. The polynucleotide of claim 2 which encodes an aspartate aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:29.

30. The polynucleotide of claim 2 which encodes an glucosamine:fructose-6-phosphate aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:30.

31. The polynucleotide of claim 2 which encodes an histidinol-phosphate aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:31.

32. The polynucleotide of claim 2 which encodes a branched chain aminotransferase that is at least 70% identical to the enzyme of SEQ ID NO:32.

33. An isolated polynucleotide encoding an enzyme with aminotransferases activity, wherein the polynucleotides encodes the enzyme of SEQ ID NOS:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, or SEQ ID NO:32.

34. An isolated polynucleotide of claim 1, wherein the enzyme encoded by the isolated polynucleotide has the same amino group acceptor and amino group donor specificity as the enzyme to which it is at least 70% identical.

35. A nucleic acid probe complementary to the nucleic acid probe of claim 17.--